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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
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| 09/333,159 | 06/14/99 | MCCARTHY S | 10147-6 |

000570 HM12/0913
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| EXAMINER | |
|---|---|
| TIANG, D. | |
| **ART UNIT** | **PAPER NUMBER** |
| 1646 | 7 |

**DATE MAILED:** 09/13/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

| Office Action Summary | Application No. 09/333,159 | Applicant(s) MCCARTHY ET AL. | |
|---|---|---|---|
| | Examiner Dong Jiang | Art Unit 1646 | |

*-- The MAILING DATE of this communication appears on the cov r sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *16 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-7,12 and 24-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,12 and 24-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED OFFICE ACTION

Applicant's election without traverse of Invention A, claims 1-7 and 12 in Paper No. 6, filed on 16 August 2001 is acknowledged. Applicant's species election with traverse of SEQ ID NO:45 in Paper No. 6 is acknowledged. The traversal is on the ground(s) that SEQ ID NO:45 is the nucleotide sequence of a cDNA that entirely contains SEQ ID NO:46, which is the nucleotide sequence of the open reading frame of the cDNA. This argument is persuasive, and requirement for the species restriction between SEQ ID NO:45 and 46 is withdrawn.

Applicant's preliminary amendment in paper No. 6 is acknowledged and entered. Following the amendment, the original claims 8-11 and 13-23 are canceled, claims 1, 2, and 12 are amended, and the new claims 24-38 are added.

Currently claims 1-7, 12, and 24-38 are pending and under consideration.

The references listed on the PTO-1449 in paper No. 4 are not present in the current application file. In response to this Office Action, only applicants may submit another set of the same references, and the Examiner will consider them as though they were submitted with IDS in paper No. 4.

***Formal Matters:***

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

The first two inventors did not sign their name in full.

***Objections and Rejections under 35 U.S.C. §101 and §112:***

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-7, 12, and 24-38 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a credible, substantial, specific, or well-established utility.

Claims 1-7, 12, and 24-38 are directed to isolated nucleic acid sequences of SEQ ID NO:45 and 46 encoding polypeptide of SEQ ID NO:47, fragments thereof, vectors containing same, host cells thereof, and a method of recombinantly producing the encoded polypeptide, which is designated TANGO294.

The specification discloses the polynucleotide sequences with SEQ ID NO:45 and 46, which encode a human TANGO294 having SEQ ID NO:47. The specification asserts that TANGO294 protein is involved in facilitating absorption and metabolism of fat, thus, can be used to prevent, diagnose, and treat disorders involving one or more physiological activities mediated by TANGO294 protein. Such disorders include, for example, inadequate expression of gastric/pancreatic lipase, cystic fibrosis, exocrine pancreatic insufficiency, fat malabsorption, obesity, and the like (page 8, the second paragraph).

The asserted utilities discussed above are not considered to be credible because such assertion is based on that human TANGO294 protein exhibits considerable sequence similarity to lingual and gastric lipase proteins of rat, dog, and human (page 64, lines 11-15). As stated in the specification, the sequence similarity of TANGO294 and mammalian lingual, gastric, and lysosomal acid lipase proteins indicates that TANGO294 is involved in facilitating absorption and metabolism of fat (page 65, lines 15-18). Such prediction based upon sequence similarity of known proteins is not credible, and cannot be accepted in the absence of supporting evidence, because it is well known that many proteins belong to a same family, share a high degree of sequence similarity, yet have diverse, and sometimes even opposite biological activities and functions. For example, in the transforming growth factor (TGF) family, Vukicevic et al. (1996. PNAS USA 93:9021-9026) disclose that OP-1, a member of the TGF-family of proteins, has the ability to induce metanephrogenesis, whereas closely related TGF- family members BMP-2 and TGF-1 had no effect on metanephrogenesis under identical conditions (p. 9023, paragraph bridging columns 1-2). Additionally, Skolnick et al. (Trends in Biotechnology, 2000) teaches that because proteins can have similar structures but different functions, determining the structure of a protein may not necessarily reveal its function (see entire article, especially Box 2).

Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologues must have different molecular and cellular functions. Therefore, in the absence of any actual experimental confirmation of any of biological properties, the skilled artisan would not accept the asserted activity as being credible, even though the assertion that TANGO294 may be a lingual, gastric lipase, and involved in facilitating absorption and metabolism of fat is specific, and substantial.

Therefore, each of the disclosed utilities requires additional knowledge about the claimed nucleic acids and the protein encoded thereby before the nucleic acids or protein can be used for a specific purpose, such as those set forth in the specification. The specification does not provide any of such specific information about SEQ ID NO:45, 46, or 47. The disclosed uses in diagnosis, drug development, and treatment are not credible, in the absence of knowledge of the substrate which said TANGO294 bind, any disclosed gene mutation, or any disease or condition which could be so diagnosed, or treated. Therefore, there is no immediately available patentable utility for TANGO294 or nucleic acids encoding such. Upon further research, a credible utility might be found for the claimed isolated polynucleotides and the protein. This further characterization, however, is part of the act of invention, and until it has been undertaken, the claimed invention is incomplete.

Other generalized utilities asserted for all polynucleotides and polypeptides in the specification are noted, such as that the claimed polynucleotides and polypeptides can be used in screening assays, detection assays, predictive assays (diagnosis, prognosis, etc.), and treatment (page 108, lines 17-22). The specification teaches that the polynucleotides can be used as a probe or primer in chromosome mapping, tissue typing, forensic identification (page 116, B), and detecting genetic lesions or mutations in the gene (page 125, the last paragraph). The specification further teaches that The polypeptide of the invention can be used in screening compounds and drug development (page 109, A.). The nucleic acids, the polypeptides, and antibodies thereto, along with compounds identified, are stated to be useful in detecting expression levels (mRNA or protein), or activity (page 121, 1. to page 123), identifying subjects having or at risk of developing a disease or disorder associated with aberrant expression or activity of the polypeptide of the invention (page 124, lines 20-22). However, until a credible

utility can be attributed to TANGO294, or a credible disease association established, those uses are not considered to be a specific or substantial utility, as such uses could be asserted for *any* polypeptide or protein.

The instant situation is analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. ... a patent is not a hunting license. ....[i]t is not a reward for the search, but compensation for its successful conclusion.

The instant claims are drawn to polynucleotides encoding proteins of as yet undetermined function or biological significance. There is no evidence of record or any line of reasoning that would support a conclusion that the claimed nucleic acids encoding TANGO294 were, as of the filing date, useful for diagnosis and treatment of any of disorders as stated at page 8 (lines 8-10) of the specification. Until some actual and specific biological significance can be attributed to the polynucleotides or the polypeptide identified in the specification as TANGO294, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility and the claimed invention is incomplete as of the filing date.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 12, and 24-38 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Furthermore, even if the specification taught how to use human TANGO294, enablement would not be commensurate in scope with claim 1, and the dependent claims 26-28, 30-33, 3-6, 34, 7, 12, 36-38, which reads on nucleic acids of SEQ ID NO:45, 46, all fragments thereof, and variants thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with the claims. The specification discloses merely one human gene and its cDNA with SEQ ID NO:45 and 46, respectively, which encodes a polypeptide of SEQ ID NO:47, or TANGO294, and provides neither guidance, nor working example to teach how to make any of variants of TANGO294. The specification indicates that a fragment of a nucleic acid sequence can be used as a probe, a primer, or to encode a biological active portion of a polypeptide of the invention (page 73, lines 25-26). However, the specification does not teach that as a probe, whether these nucleic acid fragments are specific and hybridize *only* to TANGO294 polynucleotide, or they may represent parts of conservative regions and hybridize to other members of the family. Further, the specification does not define any domain or region in TANGO294 as a "biological active portion", nor, in fact, has any specific biological activity been disclosed for TANGO294. Without knowing what the biological activity is, it would require undue experimentation to make a fragment conserving such. Additionally, the skilled artisan would not know how to use the fragments which neither is specific to TANGO294, nor encodes a "biological active portion".

Further, even if hybridization were found to have utility and be enabled for the fragments of SEQ ID NO:1, the scope would not be commensurate with the variants hybridizing to SEQ ID NO:45 or 46 under "stringent condition", which, according to the specification, include

nucleotide sequences at least 60% to each other (page 76, lines 3-6), for the same reasons addressed above.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, 12, and 24-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, part e, 7, part e, 32, and 37 are incomplete for omitting essential elements. The claims are limited by a hybridization method under "stringent conditions". The specification does not clearly define such conditions, and only provides "a prefferred, non-limiting example" of such (page 76, lines 8-11). As the target sequence is specific, an artisan needs to know the specific corresponding hybridization conditions in order to practice the claimed invention. The claim recites neither hybridization conditions to ensure that any hybridized polynucleotides will comprise specific sequence within the meaning of the disclosure, nor process steps which would effect the removal of nonspecific hybridization complexes. Without knowing accurately what conditions are comprised by "stringent" conditions, one can not determine the metes and bounds of nucleic acids within the limitations of the claim.

The remaining claims are rejected for depending from an indefinite claim.

***Rejections Over Prior Art:***

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Du et al. (locus HSU08464, GenEmble, 1994) teaches a polynucleotide sequence of a human lysosomal acid lipase, which comprises nucleic acid residues 39-1241 of SEQ ID NO:46 of the instant case with 65.4% homology (see computer printout of the search results).

***Conclusion:***

No claim is allowed.

***Advisory Information:***

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:30 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

LORRAINE SPECTOR
PRIMARY EXAMINER

DJ
8/30/01